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| 10/561,771   | 12/21/2005  | Hiromichi Yamashita  | H6808.0094/P094     | 1609             |
| 24998  | 7590        | 07/30/2009           | EXAMINER            |                  |
| DICKSTEIN SHAPIRO LLP<br>1825 EYE STREET NW<br>Washington, DC 20006-5403 |             |                      |                     | XU, XIAOYUN      |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/561,771             | YAMASHITA ET AL.    |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | ROBERT XU              | 1797                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 02 June 2009.

2a) This action is **FINAL**.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-11 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

|  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ .  | 6) <input type="checkbox"/> Other: _____ .                        |

## DETAILED ACTION

1. The amendment filed on 06/02/2009 has been entered and fully considered. Claims 1-11 are pending, of which Claims 1, 8, and 9 are amended, and Claim 11 is newly added.

### ***Response to Amendment***

2. In response to amendment, the examiner establishes 112, first and second paragraph rejection and withdraws rejection over the prior art established in the previous Office action.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The examiner respectfully reminds the Applicants that according to MPEP §2163:

"2163.02. Standard for Determining Compliance with Written Description Requirement:

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the

disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

The Applicants did not describe the ways to calculate a number of amino acid sequences for each mass in the specification "using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention", and thus they did not reasonably convey those skilled in the art that they possessed the invention recited in claims 1 and 8 at the filing date of the invention. Claim 1 recites "selecting an amino acid sequence from protein information and peptide information stored in a data base". Claim 8 recites "an amino acid sequence is selected from protein information and peptide information stored in a database". If only one amino acid sequence from protein information and peptide information stored in a database is selected, how could applicants calculate a number of amino acid sequences for each mass?

Claim 4, step B recites "estimating the mass of each of said obtained proteins". Step C recites "summing the estimated results for all of the proteins". This is not consistent with the specification disclosure. The specification discloses enzymatically digesting proteins and estimating the mass of digested peptides. Therefore, applicants does not describe the steps B and C "using such descriptive means as words,

structures, figures, diagrams, and formulas that fully set forth the claimed invention", and thus they did not reasonably convey those skilled in the art that they possessed the invention recited in claim 4 at the filing date of the invention.

Claim 6 recites "the weighting value indicates the highest value in said pattern is eliminated when the precursor ion to be subjected to MS/MS analysis is selected". The applicant discloses eliminating the mass of highest weighting value in the first pattern when the precursor ion is selected in the specification (see paragraph [0060]). However, the applicants did not describe eliminating the mass of highest weighting value in the second pattern when the precursor ion is selected in the specification "using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention", and thus they did not reasonably convey those skilled in the art that they possessed the invention recited in claim 6 at the filing date of the invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step in Claims 1, 4 and 8 is: proteolytic digestion of protein sample. Without step of proteolytic digestion of protein sample, the mass of obtained mass spectrum of protein sample will not match the mass of the theoretical proteolytic peptide of a protein in a database. The examiner suggests the following wording for consideration:

A mass spectrometric method for protein analysis, comprising:

obtaining information on masses of selected peptides from available databases with the peptides related to the class of proteins under analysis and resulted from enzymatic digestion of proteins;

calculating frequency of occurrence of masses in selected peptides with 1 for each occurrence of the mass and 0 for each non-occurrence of the mass;

calculating weight pattern based on the frequency of the masses;

performing enzymatic digestions of the proteins under analysis;

performing mass spectrometric analysis of the resulted peptides;  
selecting precursor ion based on the calculated weight pattern including 1 for each occurrence of the mass and 0 for each non-occurrence of the mass in the spectrum;

obtaining MS/MS tandem mass spectra of the selected precursor ions; and  
identifying proteins based on the results of the analysis.

8. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites “estimating each mass corresponding to each amino acid sequence information” without specifically defining the nature of the amino acid sequence, which renders the claim unclear and indefinite, since it is not apparent, as to which amino acid sequence is recited in the claim.

Claim 5, recites “a first pattern for weighting in order of decreasing frequency and a second pattern for weighting in order of increasing frequency”. It is not clear whether the weighting starts from low to high or from high to low. The examiner suggests the following wording for consideration: a first pattern, in which masses of lower frequencies are emphasized and a second pattern, in which masses of higher frequencies are emphasized.

Claim 8 recites “each mass corresponding to each amino acid sequence information is estimated” without specifically defining the nature of the amino acid sequence, which renders the claim unclear and indefinite, since it is not apparent, as to which amino acid sequence is recited in the claim.

The Applicants are respectfully referred to the following excerpt from MPEP:

**“§2171 Two Separate Requirements for Claims Under 35 U.S.C. 112, Second Paragraph:**

The second paragraph of 35 U.S.C. 112 is directed to requirements for the claims: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

There are two separate requirements set forth in this paragraph:  
(A) the claims must set forth the subject matter that applicants regard as their

invention; and  
(B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

The first requirement is a subjective one because it is dependent on what the applicants for a patent regard as their invention. The second requirement is an objective one because it is not dependent on the views of applicant or any particular individual, but is evaluated in the context of whether the claim is definite - i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art.

Although an essential purpose of the examination process is to determine whether or not the claims define an invention that is both novel and nonobvious over the prior art, another essential purpose of patent examination is to determine whether or not the claims are precise, clear, correct, and unambiguous. The uncertainties of claim scope should be removed, as much as possible, during the examination process.

The inquiry during examination is patentability of the invention as applicant regards it. If the claims do not particularly point out and distinctly claim that which applicants regard as their invention, the appropriate action by the examiner is to reject the claims under 35 U.S.C. 112, second paragraph. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). If a rejection is based on 35 U.S.C. 112, second paragraph, the examiner should further explain whether the rejection is based on indefiniteness or on the failure to claim what applicants regard as their invention. *Ex parte Ionescu*, 222 USPQ 537, 539 Bd. App. 1984)"

Furthermore:

#### **§2172 Subject Matter Which Applicants Regard as Their Invention:**

If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)."

In this case "the language of the claims is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement", and thus the rejection under 35 U.S.C. 112, second paragraph, is appropriate.

#### ***Claim Rejections - 35 USC § 102***

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. **Claims 1, 2 and 8** are rejected under 35 U.S.C. 102(a) as being anticipated by Reid et al. (Journal of Mass Spectrometry, 2002) (Reid).

In regard to Claim 1, Reid teaches a mass analysis method (see abstract). The method comprises:

selecting an amino acid sequence from protein information and peptide information stored in a database (see page 664, right col. 2<sup>nd</sup> paragraph),

estimating each mass of corresponding to each amino acid sequence information (see page 664, right col. 2<sup>nd</sup> paragraph); and

calculating a number of amino acid sequences for each mass (see page 664, right col. 2<sup>nd</sup> paragraph);

obtaining a mass spectrum by performing an MS analysis of a sample with a mass analysis apparatus after the calculating of the number of amino acid sequences (see page 664, right col. 2<sup>nd</sup> paragraph);

selecting a precursor ion based on the acquired mass spectrum and the number of amino acid sequences (see page 664, right col. 3<sup>rd</sup> paragraph; page 665, left col. 1<sup>st</sup> paragraph);

performing an MS/MS analysis of the selected precursor ion (see page 664, right col. 3<sup>rd</sup> paragraph); and

performing an identification process using a mass spectrum obtained through the MS/MS analysis (see page 665, left col. 1<sup>st</sup> paragraph).

In regard to Claim 2, Reid reviews 'bottom up' protein identification where the protein is digested by enzyme, the mass fingerprint of the peptide is compared with the database (see page 664, right col. 2<sup>nd</sup> paragraph).

In regard to Claim 8, Reid discloses a mass analysis apparatus, comprising:  
an ionization unit for ionizing a sample (see page 664, left col. Scheme 1);  
a mass analysis unit for performing mass analysis (see page 664, left col. Scheme 1); and

a data processing unit for setting analysis conditions and performing on an analysis result (see page 664, left col. Scheme 1),

wherein the data processing unit performs:

a preparation process in which in accordance with a preset condition, an amino acid sequence is selected from protein information and peptide information stored in a database, each mass corresponding to each amino acid sequence information is estimated, and a number of amino acid sequences for each mass is calculated (see page 664 right col. 2<sup>nd</sup> paragraph); and

a precursor ion selection process in which after the preparation process, a precursor ion to be subjected to MS/MS analysis is selected in light of a mass spectrum obtained through a mass analysis of an actual sample and in accordance with the number of amino acid sequences (see page 664, right col. 3<sup>rd</sup> paragraph).

Reid teaches applying tandem mass spectrometry technology to peptide ions of mass on the order of a few kilo-Daltons or less (see page 664, right col. 3<sup>rd</sup> paragraph). Reid also teaches identifying peptide, and therefore the protein of origin, by protein sequence database analysis, searching a limited stretch of amino acid sequence or sequence tag or by *de novo* sequence analysis (see page 665, left col. 1<sup>st</sup> paragraph).

### ***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. **Claims 3, 4, 7 and 9-11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Reid.

In regard to Claim 3, Reid does not specifically teach pre-setting the number of precursor ions. Reid teaches reducing the number of precursor charge states in order to reduce the complexity (see page 671, right col. 2<sup>nd</sup> paragraph). At the time of the invention it would have been obvious to ordinary skill in the art to pre-setting the number of precursor ions for the analysis, in order to reduce the complexity.

In regard to Claim 4, Reid teaches a mass analysis method where a sample is ionized and a protein is analyzed using a mass analysis apparatus, comprising:

(a) obtaining information about a plurality of protein from an external database in which information about protein is stored (see page 665, left col. 1<sup>st</sup> paragraph);

(b) estimating the mass of each of the obtained proteins (see page 664, right col. 2<sup>nd</sup> paragraph);

(c) calculating a weight pattern by conducting normalization such that 1 is given when there is the estimated mass and 0 is given when there is no such estimated mass (counting the number of peaks), summing the estimation results for all of the proteins to determine a frequency (see page 664, right col. 2<sup>nd</sup> paragraph; page 671, right col. 2<sup>nd</sup> paragraph);

(d) measuring a sample and acquiring a mass spectrum (see page 664, right col. 2<sup>nd</sup> paragraph);

Reid does not specifically teach normalizing the spectrum of the sample such that 1 is given when there is a mass and 0 is given when there is no mass. However, such normalization is obvious to ordinary skill in the art, because 1 means a peak for a mass and 0 means no peak for a mass in a spectrum. It is another way of describing peaks in a spectrum.

Reid does not specifically teach creating a pseudospectrum by superposing the spectrum of an actual sample with a weight pattern from a database. However, Reid teaches comparing the spectrum of an actual sample with a weight pattern database. It would have been obvious to ordinary skill in the art to superposing the spectrum of an

actual sample with a weight pattern from a database, because that is means for comparing the spectrum with database.

Reid teaches selecting precursor ion to be subjected to MS/MS analysis from the mass spectrum of the sample based on comparing the spectrum of an actual sample with a weight pattern database (see page 671, right col. 2<sup>nd</sup> paragraph).

In regard to Claim 7, Reid teaches obtaining new weight pattern based on information from the database and the difference in frequency of the weight patterns (see page 671, right col. 2<sup>nd</sup> paragraph).

In regard to Claims 9 and 10, Reid does not disclose a display unit to display sequence information for each of the masses and superimpose with the mass spectrum. Reid teaches database interrogation and amino acid sequence searching (see page 665, left col. 1<sup>st</sup> paragraph) as well as computer display unit (see Plate 1). It would have been obvious to one of ordinary skill in the art to display the spectrum and frequency information on the displaying unit.

In regard to Claim 11, Reid teaches selecting precursor ion in order of decreasing intensity in a range of intensity of mass spectrum (see page 671, right col. 2<sup>nd</sup> paragraph).

### ***Response to Arguments***

15. Applicant's arguments filed on 06/02/2009 have been fully considered but they are not persuasive.

The examiner's rejection is based on the broadest interpretation of the claims in light of the specification, not reading the specification into the claim.

When Reid calculates the mass of the peptides, he automatically calculates the number of peptides to the mass. When Reid select precursor ion for MS/MS, the there might be one or more peptides sequence in the database that matches the mass of the precursor ion. Therefore, Reid selects precursor ion based on the obtained mass spectrum and the number of amino acid sequence.

The rejection under 112, second paragraph, to Claim 6 remains, because applicants' argument is not persuasive. Paragraphs [0060]-[0062] are regarding the first

pattern not the second pattern. Paragraphs [0063]-[0065] regarding the second pattern does not teach eliminating the highest value.

***Conclusion***

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

7/29/2009

/Yelena G. Gakh/  
Primary Examiner, Art Unit 1797

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